Withdrawn Claims

For the reasons set forth below, Applicants submit that all pending claims presently subject to examination are in condition for allowance. Because the withdrawn claims depend from, and thus recite all features of, allowable claim 21, rejoinder and allowance of the withdrawn claims are respectfully requested.

Rejection Under 35 U.S.C. §103

The Office Action rejects claims 21-24 under 35 U.S.C. §103(a) over U.S. Patent Application Publication No. US 2002/0047058 to Verhoff et al. ("Verhoff") in view of U.S. Patent No. 6,753,330 to Takano et al. ("Takano"). Applicants respectfully traverse the rejection.

Claim 21 recites "[a] composition, comprising: an extremely poorly water-soluble drug; and a porous silica material; wherein: the composition is obtained by treating a mixture comprising the porous silica material and the extremely poorly water-soluble drug with a supercritical fluid or subcritical fluid of carbon dioxide; the extremely poorly water-soluble drug has a solubility in water at 25 °C of less than 10 μg/mL prior to treatment; and the porous silica material has an average pore diameter of from 1 to 20 nm, a total pore volume of pores having diameters within ±40% of the average pore diameter accounts for at least 60% of a volume of all pores of the porous silica material, and the porous silica material has an X-ray diffraction pattern including at least one peak at a position of a diffraction angle (2θ) corresponding to a *d* value of at least 1 nm" (emphasis added). Verhoff and Takano do not disclose or suggest such a composition.

Claim 21 unequivocally requires that the composition include a porous silica. As discussed during the March 2, 2010 Personal Interview, Verhoff does not disclose or suggest

a composition including a porous silica. Accordingly, Verhoff does not disclose or suggest each and every feature of claim 21.

Verhoff discloses a process for milling a solid substrate in which silica milling bodies may be used. *See* Verhoff, Abstract, paragraph [0108]. However, none of the silica milling bodies described in Verhoff are porous. Verhoff discloses:

> Useful milling media bodies include silicon dioxide in various forms such as glass beads and colloidal silica. Colloidal silica can be obtained in a number of size ranges. For example, basic colloidal silica with an average particle size of 5 nm at 15% solids and containing 0.75% Na_2O is commercially available from Eka Nobel, Inc. of Augusta, Ga. under the trade designation "NYACOL 215." Basic colloidal silica with an average particle size of 5 nm at 15% solids and containing 0.75% Na_2O is commercially available from Nalco Products, Inc. of Naperville, Ill. under the trade designation "NALCO 1115." Basic colloidal silica with an average particle size of 5 nm at 15% solids and containing NH_3 is commercially available from Nalco Products, Inc. under the trade designation "NALCO 2326." Basic colloidal silica with an average particle size of S nm at 30% solids and containing 0.65% Na_2O is commercially available from Nalco Products, Inc. under the trade designation "NALCO 1130." Acidic colloidal silica with an average particle size of 20 nm at 34% by weight solids is commercially available from Nalco Products, Inc. under the trade designation "NALCOAG 1034A." Acidic alumina-coated colloidal silica with an average particle size of 20 nm as 20% SiO_2 and 4% Al_2O_3 is commercially available from Nalco Products, Inc. under the trade designation "NALCOAG 1SJ613." Colloidal silica with an average particle size of 50 nm at 50% by weight solids is commercially available from Nyacol Products, Inc. under the trade designation "NYACOL 5050." Colloidal silica with an average particle size of 99 nm at 50% by weight solids is commercially available from Nyacol Products, Inc. under the trade designation "NYACOL 9950."

See Verhoff, paragraph [0108]. As explained in Applicants' previous response, the products described in the above-quoted passage have been renamed. *See, e.g.*, July 6, 2009 Amendment, page 8 and attachments. For example:

NYACOL 215 is now Bindzil 215;

NYACOL 5050 is no longer available;

NYACOL 9950 is now Bindzil 9950;

NALCO 1115 and NALCO 2326 are equivalent to Bindzil 215;

NALCO 1130 is equivalent to Bindzil 830;

NALCOAG 1034A is equivalent to Bindzil 2034DI; and

NALCOAG 1SJ613 is equivalent to Levasil 100S/30%.

Applicants have attached hereto Product Data Sheets (Reference 1) and Sales Specifications (Reference 2) for the existing products corresponding to the products described in the above-quoted passage of Verhoff. In addition, Applicants have attached hereto available Particle Size Data (Reference 3) for products corresponding to products identified in the above-quoted passage of Verhoff obtained from the manufacturer. Further, Applicants have prepared a Table (Reference 4) showing the correspondence between the products described in the above-quoted passage of Verhoff and the currently available products described in References 1 to 3.

What is apparent from all of the materials discussed above is that all of the silica materials described in Verhoff are colloidal silicas. As is well-understood by those of ordinary skill in the art, colloidal silicas are non-porous. *See, e.g.,* JP 2008-009348, page 8, lines 42-44 (Reference 5) ("Silica particles with pores have a lower refractive index of 1.20 to 1.45 as compared to general colloidal silica particles, which have no pores, having a refractive index of about 1.46") (copy attached hereto). Claim 21 clearly requires a porous silica. Accordingly, Verhoff fails to disclose each and every feature of claim 21.

Because Verhoff employs non-porous colloidal silica, even if an active substance was milled with the colloidal silica in the presence of a super- or sub-critical fluid of carbon dioxide, the silica would not be capable of carrying the active substance and a product having improved solubility would not be obtained. This is shown, for example, in the Declaration Under 37 C.F.R. §1.132 filed in U.S. Patent Application No. 10/551,901 on June 29, 2009

("Declaration") (copy attached). In the Declaration, two compositions were prepared and subjected to a dissolution test similar to the dissolution test in the Examples of the specification in U.S. Patent Application No. 10/551,901. The compositions that were tested in the Declaration included a composition including a porous silica that did not have the average pore diameter required in claim 21 (Example 1), and a composition including a non-porous silica (Example 2). *See* Declaration, page 2. As is evident from the results shown in the TABLE in the Declaration and Table 1 in the present specification, a composition including a porous silica having the characteristics required by claim 21 yields a composition having far superior solubility. *See* Declaration, TABLE; present specification, Table 1. These results confirm that the composition of claim 21, which requires a porous silica, has a dramatically different composition/structure from any product obtained according to Verhoff.

As explained above, the colloidal silica materials of Verhoff have no pores and exist in a colloidal state. Colloidal silica materials have various uses. For example, colloidal silica materials may be used as polishing agents, processing aids for food and beverages, binders for catalysts, agents employed in investment casing shell systems, refractory binders, etc. *See* Excerpt from Nalco Company Website (Reference 6) (copy attached). There is nothing in Verhoff that would have led a skilled artisan to believe that the employed colloidal silica materials could or should be replaced with a porous silica, as in claim 21. The only indication that porous silica materials could or should be used to improve the solubility of extremely low-solubility drugs is found in the present specification.

For the reasons discussed above, Verhoff fails to disclose or suggest each and every feature of claim 21. Takano does not remedy the deficiencies of Verhoff. Takano is cited for its alleged disclosure of a pharmaceutical solid dispersions including 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one. *See* Office Action, pages 6 to 7. However, Takano, like Verhoff fails to disclose or suggest a composition including a

porous silica material as recited in claim 21. Accordingly, the combination of references fails to disclose or suggest each and every feature of claim 21.

As explained, claim 21 would not have been rendered obvious by Verhoff and Takano. Claims 22-24 depend from claim 21 and, thus, also would not have been rendered obvious by Verhoff and Takano. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Request for Information

Applicants have attached, for the Examiner's convenience, a copy of the Declaration previously submitted in response to the Request for Information set forth in the Office Action.

Conclusion

For the foregoing reasons, Applicants submit that claims 21-35 are in condition for allowance. Prompt reconsideration and allowance are respectfully requested.

Respectfully submitted,

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Attachments:

Product Data Sheets (Reference 1)
Sales Specifications (Reference 2)
Particle Size Data (Reference 3)
Table (Reference 4)
JP 2008-009348 (Reference 5)
Excerpt from Nalco Company Website (Reference 6)
Declaration 37 C.F.R. §1.132 filed in U.S. Patent Application No. 10/551,901 on June 29, 2009
Declaration Submitted in Response to Request for Information